

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
23 October 2003 (23.10.2003)

PCT

(10) International Publication Number
WO 03/087106 A1

- (51) International Patent Classification⁷: **C07D 521/00, A61K 31/4196, A61P 31/10**
- (21) International Application Number: **PCT/IB02/01197**
- (22) International Filing Date: **12 April 2002 (12.04.2002)**
- (25) Filing Language: **English**
- (26) Publication Language: **English**
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- (81) Designated States (*national*): **AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.**
- (84) Designated States (*regional*): **ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).**

Published:

— *with international search report*

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

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(54) Title: **DERIVATIVES OF 2,2,4-TRISUBSTITUTED TETRAHYDROFURAN AS ANTIFUNGAL AGENTS**

(57) Abstract: **The present invention relates to derivatives of 2,2,4-trisubstituted tetrahydrofuran as potential antifungal agents. This invention also relates to pharmaceutical compositions containing the compounds of the present invention and their use in treating and/or preventing the fungal infections in mammals, preferably humans.**

INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01197

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D521/00 A61K31/4196 A31P31/10

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A31K A31P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the International search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, BEILSTEIN Data, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	EP 0 539 938 A (SCHERING CORP) 5 May 1993 (1993-05-05) Abstract; claim 1. --- -/--	1-13

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
- *Z* document member of the same patent family

Date of the actual completion of the International search

29 August 2002

Date of mailing of the International search report

05/09/2002

Name and mailing address of the ISA

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INTERNATIONAL SEARCH REPORT

International Application No

PCT/IB 02/01197

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KITAZAKI T ET AL: "OPTICALLY ACTIVE ANTIFUNGAL AZOLES. VI.1) SYNTHESIS AND ANTIFUNGAL ACTIVITY OF N-U(1R,2R)-2-(2,4-DIFLUOROPHENYL)-2-HYDROXY-1-METHYL-3-(1H-1,2,4-TRIAZOL-1-YL)PROPYL-N'-(4-SUBSTITUTED PHENYL)-3(2H,4H)-1,2,4-TRIAZOLONES AND 5(1H,4H)-TETRAZOLONES" CHEMICAL AND PHARMACEUTICAL BULLETIN, PHARMACEUTICAL SOCIETY OF JAPAN. TOKYO, JP, vol. 44, no. 2, 1996, pages 314-327, XP002067032 ISSN: 0009-2363 Page 314, formulae I, II, 1-3. ---	1-13
X	SAAG M S ET AL: "AZOLE ANTIFUNGAL AGENTS: EMPHASIS ON NEW TRIAZOLES" ANTIMICROBIAL AGENTS AND CHEMOTHERAPY, AMERICAN SOCIETY FOR MICROBIOLOGY, WASHINGTON, DC, US, vol. 32, no. 1, 1988, pages 1-8, XP000605684 ISSN: 0066-4804 -----	1,6
Y	Page 2: paragraph "Structur". -----	2-5,7-13

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1,5,6,8 (all part)

Claim 1, 5-6 and 8 relate to compounds (I) as well as to prodrugs and metabolites thereof. Thus, these claims encompass compounds i.e. prodrugs and metabolites having structures and formulae different from those compounds represented by formula (I). Neither from the description nor from the claims it is apparent which structural features found in formula (I) must necessarily be present in said prodrugs and metabolites, and which structural features may be varied. Therefore, the scope of the claims 1, 5, 6, and 8 is so unclear (Article 6 PCT), that these claims have not been searched insofar as the terms prodrugs and metabolites are concerned.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

International application No.
PCT/IB 02/01197

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 6 and 7 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.: 1,5,6,8 (all part)
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/IB 02/01197

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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